Remarks

I. Status of Claims

Claims 1-78 are pending in the present application and claims 1-24, 58-60 and 62 have been examined. Claims 1-15, 17-19, 21-23, and 58-60 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-15, 17-19, 21-23, and 58-60 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 41-43 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skill in the art that the inventors, at the time the application was filed, had possession of the claimed invention. In a telephone call from Applicants' attorney, Examiner Murphy clarified that this was an error and the rejection was intended to be directed to claims 1-15, 17-19, 21-23, and 58-60.

Claim 62 is also stands rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-15, 17-19, 21-23, and 58-60 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

Claims 1-12, 14-15, 17-19, 21-23 and 58-59 stand rejected under 35 U.S.C. §102(b) as anticipated by PCT Publication WO 99/07832.

Claims 16, 20 and 24 have been allowed.

Claims 1, 3, and 13-15 have been amended. Support for the amendments to claim 1 is found throughout the specification as filed, for example on page 1, lines 9-10; page 1, line 29 through page 2, line 3; page 9, lines 20-22; page 10, lines 3-7 and on page 31, lines 22-25.

Support for the amendment to claim 3 is found throughout the specification as filed, in the Figures and in the Sequence Listing.

Support for the amendment to claim 13 is found throughout the specification as filed, for example on page 10, lines 3-7 and on page 31, lines 22-25.

Support for the amendment to claim 14 is found throughout the specification as filed, for example on page 14, lines 15-19.

Support for the amendment to claim 15 is found throughout the specification as filed, for example on page 14, lines 8-14.

Claims 25-57, 61 and 63-78 have been cancelled.

II. The Restriction Requirement

Although applicants do not agree with the Patent Office's analysis and treatment of the Restriction Requirement, applicants have cancelled claims 25-57, 61, and 63-78 as drawn to non-elected inventions. Applicants retain the right to file one or more divisional applications directed to non-elected subject matter.

III. Response to the Rejection of 1-15, 17-19, 21-23 and 58-60 Under 35 U.S.C. §112, First Paragraph

The Patent Office rejected claims 1-15, 17-19, 21-23 and 58-60 under 35 U.S.C. §112, first paragraph. After careful consideration of the rejection, applicants respectfully traverse the rejection and submit the following comments.

It is the Patent Office's position that the specification "does not reasonably provide enablement for a polynucleotide encoding a KCNQ5 protein, nucleic acids which are 80% identical to SEQ ID NO:1, polynucleotides which hybridize to a nucleic acid encoding SEQ ID NO:2, a polynucleotide which is an allelic variant or a splice exon variant of the polynucleotide encoding the protein encoded by SEQ ID NO:1." *Official Action*, page 3. The Patent Office concludes "[t]he specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims." *Official Action*, page 3. Summarily, it is the Patent Office's position that the claims "are overly broad since insufficient guidance is provided as to which of the myriad [of] polynucleotides which the claims encompass, will retain the characteristics of KCNQ5 activity." *Official Action*, page 3.

With regard to the enablement requirement, applicants submit that, as a matter of Patent Office practice, the burden rests upon the Patent Office to establish a *prima facie* case of a failure to comply with 35 U.S.C. § 112, first paragraph, with respect to the invention described and claimed in applicants' presumptively enabling patent application. *In re Marzocchi*, 58 C.C.P.A. 1069, 439 F.2d

220, 169 U.S.P.Q. 367 (C.C.P.A. 1971), *In re Wertheim*, 541 F.2d 257, 263, 191 U.S.P.Q. 90, 97 (C.C.P.A. 1976). More specifically, the Patent Office bears the burden of establishing by a preponderance of evidence that one of ordinary skill in the art would not be enabled to practice the present invention after considering the present disclosure in combination with what is known in the art. Applicants respectfully submit the Patent Office has not met its burden in the present case.

Indeed, 35 U.S.C. §112, first paragraph, requires no more than a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of the claims, and this requirement has clearly been met. Accordingly, claims 1-15, 17-19, 21-23 and 58-60 are in compliance with 35 U.S.C. §112, first paragraph. Withdrawal of this rejection of these claims is respectfully requested.

In support of its rejection, the Patent Office offers an "undue experimentation" analysis. Applicants address each point of the Patent Office's "undue experimentation" analysis in turn. Applicants submit that the following comments are applicable to all variants of the present invention, including nucleic acids which are 80% identical to SEQ ID NO:1, polynucleotides which hybridize to a nucleic acid encoding SEQ ID NO:2, a polynucleotide which is an allelic variant or a splice exon variant of the polynucleotide encoding the protein encoded by SEQ ID NO:1, as identified in the Patent Office's rejection of the claims.

In points 1 and 2 of its analysis (Breadth of the Claims and Nature of the Invention), the Patent Office states the present invention comprises a polynucleotide and that the claims encompass to nucleotides which encode variant KCNQ5 proteins. Applicants concur with this aspect of the Patent Office's analysis, although applicants note the invention is not limited to nucleotides encoding variant proteins, since a nucleic acid sequence encoding a KCNQ5 polypeptide itself forms an aspect of the present invention.

In point 3 of its analysis (State of the Prior Art), the Patent Office cites the Voet et al. reference (Voet et al., Biochemistry, John Wiley & Sons, (1990) pp. 126-128 and 228-234) in support of the Patent Office's contention that "detailed information regarding the structural and functional requirements of the encoded proteins are lacking, [and] it is unpredictable as to which encoding variations, if any, meet the limitations of the claims." *Official Action*, pages 4-5. Applicants disagree with the Patent Office on this point and respectfully submit that the Patent Office is not affording due weight to what is known in the art. Applicants submit that the level of skill in the areas of protein engineering and molecular biology are high. While it is true that a single

point mutation can cause a dramatic effect on a given polypeptide, the field recognizes that polypeptides are also very tolerant of mutations. Those of ordinary skill in the art would readily be able to identify mutations likely to introduce desired (or undesired) properties into the claimed polypeptides. Those of ordinary skill in the art will be aware not only of the literature in this area, which is voluminous, but also other resources that can assist in selecting a mutation. For example, guidance in determining which amino acid residues may be substituted, inserted, or deleted with or without abolishing a given biological or immunological activity can be found using computer programs well-known in the art and routinely employed for these purposes, such as the PROTEAN module of the LASERGENE software available from DNASTAR, Inc., of Madison, Wisconsin.

Thus, using the specification as a guide, coupled with what is known in the art and the sequences presented in the instant patent application, one of ordinary skill in the art could readily prepare KCNQ5 variants that would reflect the activities and/or features characteristic of KCNQ5, such as biological activity and other characteristics that are described in the specification. Alternatively, if it is desired that a KCNQ5 polypeptide exhibit properties different from those normally associated with a KCNQ5 polypeptide, this knowledge and the available resources could be employed to accomplish this goal as well. Such analyses are performed regularly by researchers in the field and involve routine application of fundamental principles and available tools. Applicants submit that the Patent Office has focused its analysis on a singular case, while overlooking the vast numbers of cases in which a protein has tolerated one or more introduced mutations in its assessment of the state of the prior art. Summarily, applicants respectfully submit that in formulating its rejection, the Patent Office has not given due weight to the level of skill in the art, to the resources now available, and to the guidance provided in the specification with respect to designing and predicting the function of variants of KCNQ5.

The Patent Office argues in point 5 of its analysis (Level of Predictability in the Art), that the Voet et al. reference demonstrates the unpredictability of the protein art. Applicants respond by reiterating the arguments presented above related to the Patent Office's treatment of the Voet et al. reference. Summarily, it is applicants' position that the Patent Office has extrapolated the single case presented in the Voet et al. reference to the conclusion that entire field of protein engineering is unpredictable. Applicants submit that this extrapolation is specious and is not supported by the reference relied upon by the Patent Office, nor by the protein biochemical literature.

Turning to the Patent Office's analysis of point 6 of its analysis (Amount of Direction Provided by the Inventor), the Patent Office is apparently contending that because applicants do not explicitly point out which residues are tolerant of substitution, the present invention is merely an invitation for further experimentation. Summarizing its position, the Patent Office states "[a]pplicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of KCNQ5." *Official Action*, page 5.

Applicants initially note that it appears that in this point (and in the subsequent point) in its analysis, the Patent Office is requiring working examples. As the Patent Office is aware, there is no legal requirement that applicants provide any examples, either working examples or prophetic examples.

Continuing, as argued above, applicants submit that using available software and other resources, coupled with an understanding of protein chemistry and related techniques, one of ordinary skill in the art could readily identify positions of the claimed KCNQ5 protein that would be tolerant of a given mutation, including additions or deletions, using the present disclosure as a guide. For example, the commercially-available software packages permit a researcher to predict the presence and nature of secondary structure, the hydropathy profile of a region, and other properties as well, based on a single primary sequence. Applicants submit that in view of the availability of appropriate literature and software tools, as well as the level of guidance provided in the specification, one of ordinary skill in the art would be able to design and produce a variant comprising a desired mutation yet retaining KCNQ5 biological activity.

In point 7 of its analysis (Existence of Working Examples), the Patent Office states no working examples are provided for variant polynucleotides encoding SEQ ID NO:2. Applicants again note that although the existence of working examples can form an element of an analysis, there is no legal requirement that applicants provide working examples.

Lastly, in point 8 of its analysis (Quantity of Experimentation Needed to Make or Use the Invention Based on the Content of the Disclosure), the Patent Office argues that a large quantity of experimentation would be required to generate the "infinite number of derivatives recited in the claims." Again, applicants submit that the Patent Office has not accorded due weight to the level of skill and the advanced state of the art. As applicants have argued above, little, if any, experimentation would be required to identify suitable residues for mutation, since many features of each residue (e.g., contribution to secondary structure, polarity, charge, hydrophobicity, etc.) can be

conveniently determined using art-recognized techniques. Even assuming, *arguendo*, that any experimentation would be required, for one of ordinary skill in the art such experimentation would be routine, given the guidance provided by the specification, the high level of skill in the pertinent art and the available resources.

Summarily, applicants submit that the Patent Office's contention that undue experimentation would be required for one of ordinary skill in the art to practice the invention commensurate with the claims is not tenable, in view of the state of the art and the guidance provided in the specification. Applicants again submit that even assuming, strictly for the purposes of argument, that a quantity of experimentation is required, the claims still comply with the requirement of 35 U.S.C. §112, first paragraph, since any such experimentation would be routine. Additionally, the relevant case law has made it clear that some experimentation is permissible.

The Patent Office contends in the Official Action that it would require a "large quantity of experimentation . . . to generate the infinite number of derivatives recited in the claims". *Official Action*, page 6. However, courts have not equated "a large amount of experimentation" with an "undue amount of experimentation". Indeed, even if it might require some experimentation to arrive at and/or characterize KCNQ5 variants, the quantity of experimentation to be performed by one skilled in the art is only one factor involved in determining whether "undue experimentation" is required to make and use the invention. "[A]n extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." *In re Colianni*, 561 F.2d 220, 224 (C.C.P.A. 1977). Applicants submit that the specification provides sufficient guidance. As courts have held, "[t]he test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). While disagreeing that any experimentation is necessary to practice the present invention commensurate with the claims, applicants submit that the experimentation suggested by the Patent Office would be considered routine and thus would clearly not be "undue."

Applicants respectfully submit that in formulating its rejection of the claims, an inappropriate standard for measuring enablement under 35 U.S.C. §112, first paragraph has been adopted. The appropriate standard is that the claimed invention must be enabled so that a person skilled in the art can make and use the invention from the disclosures of the specification, coupled with information

known in the art, without "undue experimentation". *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988). Applicants have clearly met this standard, in view of the disclosure presented in the specification and in view of the high level of skill in the art. No undue experimentation is required to practice the present invention commensurate with the claims. Applicants therefore submit claims 1-15, 17-19, 21-23 and 58-60 are in full compliance with 35 U.S.C. §112, first paragraph. Applicants further submit claims 1-15, 17-19, 21-23 and 58-60 are in condition for allowance and respectfully request the same.

IV. Response to the Rejection of Claims 1-15, 17-19, 21-23 and 58-60 Under 35 U.S.C. §112, First Paragraph

Applicants note that claims 41-43 are drawn to a non-elected invention. Applicants' attorney thanks Examiner Murphy for clarifying, in a telephone conversation on July 22, 2003, that the rejection under 35 U.S.C. §112, first paragraph, was intended to refer to claims 1-15, 17-19, 21-23 and 58-60. The following comments are, therefore, directed to claims 1-15, 17-19, 21-23 and 58-60. Applicants traverse the rejection and submit the following comments.

IV.A. Response to the Rejection of Claims 1-15, 17-19, 21-23 and 58-60

It is the Patent Office's position that the genus encompassed by the claims includes a KCNQ5 protein, nucleic acids that are 80% identical to SEQ ID NO:1, polynucleotides that hybridize to a nucleic acid encoding SEQ ID NO:2, a polynucleotide that is an allelic variant and a splice exon variant of the polynucleotide encoding the protein encoded by SEQ ID NO:1. The Patent Office reasons that the term "KCNQ5 polypeptide" is defined as encompassing mutant forms of KCNQ5, such as those having a substitution, deletion, insertion, inversion or addition. The Patent Office concludes, "[s]ince the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant one or ordinary skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus." *Official Action*, page 7.

The Patent Office contends "the claims encompass nucleotides which encode variant proteins. The specification and claim do not indicate what distinguishing attributes [are] shared by the members of the genus." *Official Action*, page 7. Applicants have amended claim 1 to recite the

element that the encoded polypeptide comprises a biologically active human KCNQ5 protein. Applicants note that the term "biologically active" is defined in the specification, particularly on page 10, lines 3-10. Applicants submit that by including this explicit language, claim 1 recites the distinguishing attributes shared by members of the genus, namely biological activity. The added claim element is read into claims 2-12, which depend from claim 1. Analogous provisions have been included by amendment into claims 13, 14 and 15. Thus, the rejected claims now include a distinguishing attribute, namely biological activity.

The Patent Office then argues "[t]he specification and the claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to SEQ ID NO:1." Applicants believe the Patent Office intended to refer to SEQ ID NO:2, which is a polypeptide sequence, while SEQ ID NO:1 is a nucleic acid sequence. Regardless, applicants again submit that the explicit recitation that an encoded polypeptide exhibit biological activity renders the Patent Office's rejection moot because, although the precise number and nature of mutations introduced into SEQ ID NO:2 is variable, the encoded polypeptide will still retain a degree of biological activity, thereby distinguishing the members of the claimed genus from those of the class of proteins.

The Patent Office contends "the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted." *Official Action*, page 7. The Patent Office further contends "[s]tructural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus." *Official Action*, page 7. Applicants submit that in view of the amendment to claims 1, 13, 14 and 15, which adds the element that the encoded polypeptide exhibit a degree of biological activity and is clearly defined in the specification, the genus is adequately described and there is a common feature of the genus members that distinguishes the members from other members of the protein class. Although a degree of variation in structure of the genus members is permitted by the claims, applicants submit that the recitation of precise structural features is not required to comply with 35 U.S.C. §112, first paragraph. Indeed, applicants submit that there the only requirement mandated by the statute is that the claims be described in such a way as to communicate to those of ordinary skill in the art that the applicant was in possession of the claimed invention. Given the amendments to claims 1 and 13-15,

coupled with the guidance provided in the specification, for example the discussion of representative conservative substitutions, applicants submit that the claims satisfy this requirement.

It is the Patent Office's position that "the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant one of ordinary skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus." *Official Action*, page 8. As applicants have stated herein above, claims 1 and 13-15 have been amended to recite the element that the claimed nucleic acid molecules exhibit the characteristic of biological activity. This property identifies the members of the genus and distinguishes them from other members of the class of proteins. Applicants further note that the specification provides guidance with regard to various substitutions that can be made (see, e.g., page 20, lines 1-28). Applicants also note that the level of skill in the art in the areas of protein chemistry and molecular biology are high.

Applicants submit that in view of the amendments to claims 1, and 13-15, claims 1-15, 17-19 21-23 and 58-60 meet the written description requirement of 35 U.S.C. §112, first paragraph. General procedures for making variants are known in the art and a ligand binding assay is provided in the specification, which can be employed, for example, in an identification of biologically active KCNQ5 polypeptides. Applicants further submit that in view of the above, one of ordinary skill in the art, upon consideration of the specification, would conclude applicants are in possession of the claimed invention. In this regard, applicants note that courts have repeatedly held that the question of whether the written description requirement is met depends on what a person of ordinary skill in the art would understand, based on consideration of the specification, and not on the explicit disclosure of particular embodiments. See, e.g., *Union Oil Company of California v. Atlantic Richfield Company*, 208 F.3d 989 (Fed. Cir. 2000); *In re Hayes Microcomputer Prods., Inc.*, 982 F.2d 1527 (Fed. Cir. 1992).

Next, applicants draw attention to the statement in the Written Description Guidelines that "[g]enerally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosures necessary to satisfy the written description requirement." *Guidelines for Examination of Patent Applications Under the 35 USC 112, ¶1 "Written Description" Requirement*, 66 Fed. Reg. 1099, 1105 (Jan. 5, 2001). As noted, methods of making the variants of the present invention are known in the art and are disclosed in the specification. The level of skill in the art is very high. Consequently, applicants submit that in view of the disclosure of the

specification, coupled with the high level of skill in the art, the claims meet the written description requirement of 35 U.S.C. §112, first paragraph.

Summarily, applicants submit that one of ordinary skill in the art would recognize that applicants had invented what was claimed, which is the standard against which the adequacy of a written description is gauged. See, e.g., *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555 (Fed. Cir. 1991) and *In re Alton*, 76 F.3d 1168, 1175 (Fed. Cir. 1996) ("If a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met."). Applicants respectfully submit that claims 1-15, 17-19, 21-23 and 58-60 meet the requirements of 35 U.S.C. §112, first paragraph. Accordingly, applicants request that the rejection of claims 1-15, 17-19, 21-23 and 58-60 under 35 U.S.C. §112, first paragraph, be reconsidered and withdrawn. Applicants further submit that claims 1-15, 17-19, 21-23 and 58-60 are in condition for allowance and respectfully solicit the same.

IV.B. Response to the Rejection of Claims 7-12

The Patent Office has rejected claims 7-12 under 35 U.S.C. §112, first paragraph, because it is the Patent Office's position that the specification "does not reasonably provide enablement for in vivo transfection." *Official Action*, page 8. Applicants traverse the rejection and submit the following comments.

Respectfully, applicants are unable to locate the section on page 25 to which the Patent Office refers in its conclusion that a host cell can be disposed within a host animal. In the indicated section, beginning on page 25 of the specification, applicants recite a variety of examples of representative host cells, which include host cells and cell lines derived from animals (e.g., mammals and insects), but applicants are unable to find an instance in which a statement that such host cells can be disposed within a host animal is explicitly or implicitly recited. Additionally, applicants are unable to identify a mention of *in vivo* transfection on page 25 of the specification. Applicants submit that the discussion on page 25 of the specification to which the Patent Office refers is directed to expression of KCNQ5 in cell culture and not in an *in vivo* system, although host cells can be derived from a variety of animals.

In view of the above, applicants respectfully submit that the rejection of claims 7-12 is not appropriate and request that the rejection of these claims under 35 U.S.C. §112, first paragraph, be

withdrawn. Applicants submit claims 7-12 are in condition for allowance and respectfully request the same.

IV.C. Response to the Rejection of Claim 62

The Patent Office has rejected claims 62 under 35 U.S.C. §112, first paragraph, because it is the Patent Office's position that "the specification is not fully compliant with all of the provisions for maintenance and availability of the deposited material." *Official Action*, page 9. Applicants traverse the rejection and submit the following comments.

Applicants submit herewith the requisite Statement, thereby overcoming the rejection of claim 62 under 35 U.S.C. §112, first paragraph.

In view of the above amendments and remarks, applicants submit claims 1-15, 17-19, 21-23 and 58-60 are in full compliance with 35 U.S.C. §112, first paragraph. Accordingly, applicants request that the rejection of these claims under 35 U.S.C. §112, first paragraph, be withdrawn. Applicants further submit claims 1-15, 17-19, 21-23 and 58-60 are in condition for allowance and respectfully request the same.

V. Response to the Rejection of Claims 1-15, 17-19, 21-23 and 58-60 Under 35 U.S.C. §112, Second Paragraph

The Patent Office has rejected claims 1-15, 17-19, 21-23 and 58-60 under 35 U.S.C. §112, second paragraph, as indefinite. Applicants traverse the rejection and submit the following comments.

V.A. Response to the Rejection of Claims 14-15

It is the Patent Office's position that claims 14-15 are indefinite because these claims recite the term "stringent conditions." The Patent Office contends "[t]he metes and bounds of the claim thus cannot be ascertained." *Official Action*, page 10. Applicants traverse the rejection and submit the following comments.

The Patent Office indicates that this rejection would be obviated by supplying specific conditions supported by the specification which Applicant considers to be 'moderately' or 'highly'

'stringent'." *Official Action*, page 10. Although applicants are of the position that the claims are definite as written, in view of the specification, in order to expedite prosecution of the present patent application, applicants have amended claims 14 and 15 as suggested by the Patent Office. Support for the amendments to claims 14 and 15 is found on page 14, lines 5-19.

Applicants submit that, in view of these amendments, claims 14-15 are definite and respectfully request that the rejection of claims 14-15 under 35 U.S.C. §112 be withdrawn and the claims allowed.

V.B. Response to the Rejection of Claim 1

The Patent Office states "[c]laim 1 is vague and indefinite in the recitation of the terms 'KCNQ5'. There is no definition within the claim to define the protein to which these acronyms refer." *Official Action*, page 10. Applicants traverse the rejection and submit the following comments.

Applicants submit that the acronym "KCNQ5" refers to KCNQ5 potassium ion channel KCNQ family member 5. Applicants further submit that this acronym is well-known in the art and has been applied to subfamily members 1-4, as indicated, for example, by the published PCT patent application cited by the Patent Office, by the references cited in the Background section of the present specification (i.e., Singh et al., (1998) *Nature Genet.* 18:25; Charlier et al., (1998) *Nature Genet.* 18:53), and by the recitation of this fact presented in the Background section of the present specification (see, e.g., page 2, lines 7-14). More particularly, "KCNQ5" is an art-recognized genomic shorthand with K representing potassium; CN channel; and Q, long QT syndrome. The 5 in KCNQ5 indicates this protein is the 5th member of the KCNQ family. See, e.g., Cooper & Jan, (2003) *Arch. Neurol.* 60:496-500, which is submitted for reference only and is attached hereto for the Patent Office's convenience. Attention is particularly directed to page 496, paragraph 3. In keeping with the established taxonomy for this family of proteins, therefore, applicants refer to the novel and newly-identified member of this gene family as KCNQ5. The claimed polypeptide and polynucleotides are referred to as such in the specification (see, e.g., page 9, lines 16-26).

It is applicants' position that claim 1 is definite as written. The term "KCNQ5" would be readily understood by those of ordinary skill in the art, as evidence by the Cooper & Jan journal article. Applicants respectfully request that the rejection of claim 1, and claims depending therefrom, under 35 U.S.C. §112 be withdrawn.

In view of the above amendments and remarks, applicants submit claims 1-15, 17-19, 21-23 and 58-60 are in full compliance with 35 U.S.C. §112, second paragraph. Accordingly, applicants request that the rejection of these claims under 35 U.S.C. §112, second paragraph, be withdrawn. Applicants further submit claims 1-15, 17-19, 21-23 and 58-60 are in condition for allowance and respectfully request the same.

VI. Response to the Rejection of Claims 1-12, 14-15, 17-19, 21-23 and 58-59 Under 35 U.S.C. §102(b)

The Patent Office has rejected claims 1-12, 14-15, 17-19, 21-23 and 58-59 under 35 U.S.C. §102(b) as anticipated by PCT Publication WO 99/07832 by Blanar et al. Applicants traverse the rejection and submit the following comments.

VI.A. Response to the Rejection of Claims 1-12, 17-19, 21-23 and 60

Summarily, it is the Patent Office's position that "[t]he nucleic acid encoding KCNQ2 anticipates claims 1 and 2 because it encodes an amino acid sequence comprising a portion of KCNQ5 of SEQ ID NO:2. Claim 3 is anticipated because the KCNQ2 polynucleotide comprises a portion of SEQ ID NO:1." *Official Action*, page 11. Applicants traverse the rejection and submit the following comments.

Applicants have amended claims 1 and 3 to remove the term "a portion." In view of this amendment to the claims, applicants submit that the cited reference, the Blanar PCT Publication does not anticipate the claims. Accordingly applicants request that the rejection of claims 1-12, 17-19, 21-23 and 60 under 35 U.S.C. §102(b) be withdrawn and the claims allowed.

VI.B. Response to the Rejection of Claims 14 and 15

The Patent Office has rejected claims 14 and 15 as anticipated because the Patent Office contends the KCNQ2 polynucleotide would hybridize under the conditions set forth in the claims to SEQ ID NO:1.

Respectfully, applicants submit that the Patent Office has not provided any concrete scientific evidence that the cited sequence would hybridize with the claimed sequence, thus anticipating the claims. It is applicants position that, given the low degree of similarity between the

two sequences in question, which is shown in the alignment provided by the Patent Office, under the claimed conditions (moderately stringent and highly stringent conditions) no such hybridization would occur. By way of example, the probe used during the isolation of the KCNQ5 gene did not hybridize to other KCNQ family members, since only KCNQ5, and not any other KCNQ family members, were isolated from the screening libraries.

Although the Patent Office has provided an alignment of a claimed polypeptide and nucleotide, this does not constitute direct evidence of the Patent Office's contention that the two sequences in question would hybridize to form a duplex, particularly since hybridization can vary with conditions. The alignment presented by the Patent Office does not rebut applicants' belief and statement that the cited KCNQ2 sequence would not hybridize to the claimed SEQ ID NO:1. Applicants submit that, absent such evidence, the Patent Office has not presented a *prima facie* case of anticipation and the rejection of the claims is improperly based solely on the Patent Office's speculation. Applicants, therefore, submit that absent any evidence to the contrary, claims 14 and 15 are not anticipated by the KCNQ2 sequence of the cited reference.

VI.C. Response to the Rejection of Claims 58-59

The Patent Office has rejected claims 58 and 59 as anticipated because the Patent Office contends KCNQ2 is an allelic variant of SEQ ID NO:1.

Applicants submit that although there is a degree of sequence similarity between the KCNQ2 and KCNQ5 (SEQ ID NO:1) sequences, the KCNQ2 sequence is not an allelic variant of KCNQ5. More particularly, the term "allelic variant" refers to an alternative form a given gene. KCNQ5 is not an alternative form of a KCNQ2 gene. These sequences are not alternative forms of the same gene as the Patent Office contends. KCNQ2 and KCNQ5 are encoded by different genes. Further, the KCNQ2 and KCNQ5 genes do not occupy the same chromosomal locus, an element of the definition of "allelic variant." In fact, the only way the two genes could be allelic variants without occupying the same chromosomal locus is as a result of a gene duplication event, which does not occur in the present case. Applicants submit that since the cited KCNQ2 sequence is not an allelic variant of KCNQ5 (SEQ ID NO:1), the cited sequence does not anticipate claims 58 and 59.

In view of the above amendments and remarks, applicants submit claims 1-12, 14-15, 17-19, 21-23 and 58-59 are in full compliance with 35 U.S.C. §102(b). Accordingly, applicants request that

the rejection of these claims under 35 U.S.C. §102(b) be withdrawn. Applicants further submit claims 1-12, 14-15, 17-19, 21-23 and 58-59 are in condition for allowance and respectfully request the same.

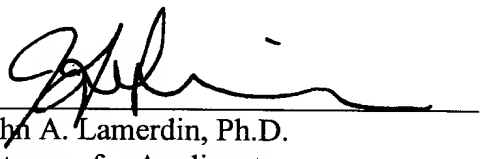
VII. Conclusions

In light of the above amendments and remarks, applicants respectfully submit that the subject patent application is now in condition for allowance and courteously solicit a Notice of Allowance.

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

Although it is believed no fee is due, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment associated with the filing of this correspondence to Deposit Account Number 19-3880 in the name of Bristol-Myers Squibb Company.

Respectfully submitted,



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